

REMARKS

Reconsideration of the Office Action mailed February 5, 2007, (hereinafter "instant Office Action") and withdrawal of the rejection of claims 21-27, 32 and 33 are respectfully requested.

In the instant Office Action, claims 1-88 are listed as pending, claims 1-20, 28-31 and 34-88 are withdrawn from consideration and claims 21-27, 32 and 33 are listed as rejected.

The Examiner has not repeated the rejection of claims 21-27, 32 and 33 under 35 U.S.C. §112, first paragraph, alleging that the specification, while being enabling for the atomic coordinates for residues 802-1124 of Tie-2 and Inhibitor III complex, allegedly does not reasonably provide enablement for the atomic coordinates of an unbound version of a Tie-2 polypeptide or atomic coordinates of the complete polypeptide of Tie-2 and Inhibitor III complex. Therefore, Applicants presume that the arguments and amendments submitted in the Request for Continued Examination filed November 17, 2006 were persuasive and the rejections have been withdrawn. Applicants respectfully request that the Examiner advise Applicants if this is not correct.

The Examiner has not repeated the rejection of Claims 21-27, 32 and 33 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the invention was filed, had possession of the claimed invention. Therefore, Applicants presume that the arguments and amendments submitted in the Request for Continued Examination filed November 17, 2006 were persuasive and the rejections have been withdrawn. Applicants respectfully request that the Examiner advise Applicants if this is not correct.

The Examiner has not repeated the rejection of claims 21, 22 and 26 under 35 U.S.C. §103(a) as allegedly being unpatentable over Chen et al (P/N 6,160,092) in view of *In re Gulack* (703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983)). Therefore, Applicants presume that the arguments and amendments submitted in the Request for Continued Examination filed November 17, 2006 were persuasive and the rejections have been withdrawn. Applicants respectfully request that the Examiner advise Applicants if this is not correct.

The Examiner has not repeated the rejection of claims 21-27 under 35 U.S.C. §103(a) as allegedly being unpatentable over Chen et al (P/N 6,160,092) in view of *In re Gulack* (703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983)), *In re Best* (195 USPQ 430) and *In re*

Fitzgerald (205 USPQ 594) and *Ziegler* (P/N 5,447,860). Therefore, Applicants presume that the arguments and amendments submitted in the Request for Continued Examination filed November 17, 2006 were persuasive and the rejections have been withdrawn. Applicants respectfully request that the Examiner advise Applicants if this is not correct.

The Examiner has not repeated the rejection of claims 21-27 under 35 U.S.C. §103(a) as being unpatentable over *Chen et al.* (P/N 6,160,092) in view of *Vikkula et al.* (Cell, 1996, Volume 87, pages 1181-1190) and *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594). Therefore, Applicants presume that the arguments and amendments submitted in the Request for Continued Examination filed November 17, 2006 were persuasive and the rejections have been withdrawn. Applicants respectfully request that the Examiner advise Applicants if this is not correct.

The Examiner has rejected claims 21-27, 32 and 33 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

The Examiner asks “[h]ow does one skilled in the art determine if a compound is an inhibitor merely by determining if it fits into an active site?” Applicants respectfully direct the Examiner’s attention to the following portions of the specification as originally filed:

- 1) Page 4, line 24 to page 5, line 3 wherein Applicants teach how the methods of the invention can be used to facilitate formation of Tie-2 crystals which enable the rational development of inhibitors of Tie-2.
- 2) Page 5, line 25 to page 6, line 2 wherein Applicants teach using the atomic coordinates derived from study of polypeptides comprising the catalytic domain of Tie-2 to identify compounds that fit in the catalytic domain.
- 3) Page 26, lines 23-28 wherein Applicants teach whether a compound fits into the catalytic domain.
- 4) Page 27, lines 3-9 wherein Applicants describe how one can identify a potential inhibitor of Tie-2 based on the ability of one or more functional groups of the compounds, when present in the Tie-2 catalytic domain, to interact with one or more subsites of the Tie-2 catalytic domain.

The instant specification teaches crystallization conditions for diphosphorylated Tie-2 802-1124 on page 48, Tie-2 (D964N) 802-1124 (SEQ ID NO 1) on page 49 and for Tie-2 (D964N) 802-11234 (SEQ ID NO 2) on page 51 of the instant application. In Example 2, Applicants have exemplified the steps of claim 21 by identifying a compound which is an inhibitor of Tie-2 by obtaining the atomic coordinates of a crystal of a polypeptide comprising the catalytic domain of a Tie-2 protein, using these atomic coordinates to define the active subsites of Tie-2 and identifying a compound which binds to one or more active subsites and inhibit the Tie-2 protein. Applicants also teach inhibitor docking in Example 2.

Further, in Examples 3 and 4, Applicants teach how to determine the *in vitro* potency of compounds in inhibiting Tie-2. Once a compound is found to bind to the active subsites, one can utilize the assays taught in the instant application to measure the ability of the compound to inhibit Tie-2. Applicants have taught all steps of claim 21 as well as how to evaluate the potency of compounds with respect to their ability to inhibit Tie-2. Therefore, claims 21-27, 32 and 33 are enabled.

Based upon the foregoing, the rejection of claims 21-27, 32 and 33 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, is obviated and should be withdrawn.

No fees are due for the instant amendment since the total number of claims after entry of the amendments hereinabove is not more than the total number of claims that Applicants have paid for to date.

Based upon the foregoing, Applicants believe that claims 21-27, 32 and 33 are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that a telephone conference would advance the condition of the instant application for allowance, Applicants invite the Examiner to call Applicants' agent at the number noted below.

Respectfully submitted,

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